UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,736	10/18/2004	Xavier Billot	MC058YP	2550
MERCK AND	7590 06/01/200 CO., INC	EXAMINER		
PO BOX 2000		BASQUILL, SEAN M		
RAHWAY, NJ 07065-0907			ART UNIT	PAPER NUMBER
			1612	
			MAIL DATE	DELIVERY MODE
			06/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief

Application No.	Applicant(s)	
10/511,736	BILLOT ET AL.	
Examiner	Art Unit	

	Sean Basquill	1612	
The MAILING DATE of this communication appe	ars on the cover sheet with the c	orrespondence add	ress
THE REPLY FILED <u>15 May 2009</u> FAILS TO PLACE THIS APPI	LICATION IN CONDITION FOR AL	LOWANCE.	
1. The reply was filed after a final rejection, but prior to or on application, applicant must timely file one of the following application in condition for allowance; (2) a Notice of Apper for Continued Examination (RCE) in compliance with 37 C periods:	replies: (1) an amendment, affidavit eal (with appeal fee) in compliance	, or other evidence, w with 37 CFR 41.31; or	hich places the (3) a Request
a) The period for reply expires <u>3</u> months from the mailing date	of the final rejection.		
b) The period for reply expires on: (1) the mailing date of this A no event, however, will the statutory period for reply expire la Examiner Note: If box 1 is checked, check either box (a) or (MONTHS OF THE FINAL REJECTION. See MPEP 706.07(the content of the co	dvisory Action, or (2) the date set forth in ter than SIX MONTHS from the mailing b). ONLY CHECK BOX (b) WHEN THE	date of the final rejection	n.
Extensions of time may be obtained under 37 CFR 1.136(a). The date of have been filed is the date for purposes of determining the period of extunder 37 CFR 1.17(a) is calculated from: (1) the expiration date of the set forth in (b) above, if checked. Any reply received by the Office later may reduce any earned patent term adjustment. See 37 CFR 1.704(b). NOTICE OF APPEAL	ension and the corresponding amount of hortened statutory period for reply origin	of the fee. The appropria nally set in the final Office	ate extension fee e action; or (2) as
 The Notice of Appeal was filed on A brief in comp filing the Notice of Appeal (37 CFR 41.37(a)), or any exter Notice of Appeal has been filed, any reply must be filed with AMENDMENTS 	nsion thereof (37 CFR 41.37(e)), to	avoid dismissal of the	
	out prior to the data of filing a brief	will not be entered be	201122
3. The proposed amendment(s) filed after a final rejection, by (a) They raise new issues that would require further cor (b) They raise the issue of new matter (see NOTE below (c) They are not deemed to place the application in beti	nsideration and/or search (see NOT w);	E below);	
appeal; and/or	ion form for appear by materially rec	idenig of enriphityning a	10 100000 101
(d) ☐ They present additional claims without canceling a c NOTE: (See 37 CFR 1.116 and 41.33(a)).	corresponding number of finally reje	ected claims.	
4. The amendments are not in compliance with 37 CFR 1.12	21. See attached Notice of Non-Cor	mpliant Amendment (I	PTOL-324).
5. Applicant's reply has overcome the following rejection(s):			,
 Newly proposed or amended claim(s) would be all non-allowable claim(s). 	owable if submitted in a separate, t	imely filed amendmer	nt canceling the
7. For purposes of appeal, the proposed amendment(s): a) [how the new or amended claims would be rejected is prov The status of the claim(s) is (or will be) as follows: Claim(s) allowed:	☐ will not be entered, or b) ☐ will ided below or appended.	be entered and an ex	xplanation of
Claim(s) objected to: Claim(s) rejected: <u>17-19,21 and 22</u> . Claim(s) withdrawn from consideration:			
AFFIDAVIT OR OTHER EVIDENCE			
 The affidavit or other evidence filed after a final action, but because applicant failed to provide a showing of good and was not earlier presented. See 37 CFR 1.116(e). 			
9. The affidavit or other evidence filed after the date of filing entered because the affidavit or other evidence failed to o showing a good and sufficient reasons why it is necessary	vercome <u>all</u> rejections under appea	l and/or appellant fails	s to provide a
10. ☐ The affidavit or other evidence is entered. An explanation REQUEST FOR RECONSIDERATION/OTHER	n of the status of the claims after er	ntry is below or attach	ed.
 The request for reconsideration has been considered but <u>See Continuation Sheet.</u> 		condition for allowan	ce because:
12. ☐ Note the attached Information <i>Disclosure Statement</i>(s). (13. ☐ Other:	PTO/SB/08) Paper No(s)		
/Frederick Krass/ Supervisory Patent Examiner, Art Unit 1612	/Sean Basquill/		

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' response to the final rejection simply reiterates the arguments the examiner has fully considered and deemed unpersuasive. As put forth in both previous office actions, the distinction between the compounds disclosed in Cameron and those of the instant Claims consists solely of a difluoro substitution on the 4 carbon of the omega chain. Similar EP4 receptor antagonists, such as those disclosed by Maruyama, describe prostaglandin derivatives similar in structure to those of both the instant Claims as well as those disclosed in Cameron wherein the 4 carbon of the omega chain carries such a difluor substition. Combined with the utility associated with these compounds disclosed by both Cameron and Maruyama, namely the prevention of bone loss, the disclosure of Cameron, taken with the disclosure of Maruyama, would suggest the desirability of introducing such a difluoro moiety at position 4 of the omega chain in the compounds disclosed by Cameron. This motivation is further supported by the knowledge possessed by one having ordinary skill in the art as represented by the Wermuth reference, namely that flourine atoms are well-recognized and commonly used substituents for hydrogen atoms in medicinal organic chemistry owing to their bioisosteric similarities. In light of the foregoing, it is clear that the artisan possessing ordinary skill in the chemical arts would recognize that substituting for the dihydro moiety of the 4 carbon of the omega chain in the compound disclosed by Cameron the difluoro moiety suggested by Maruyama and reinforced by Weymouth would lead to an EP4 receptor agonist useful in the treatment of such diseases where such compounds find utility. Absent sufficient secondary indicia of nonobviousness commensurate in scope with the invention as claimed in the instant application, the examiner's prima facie case has not been overcome.